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No. 89-1648 (2)

In the Supreme Court of the United States

OCTOBER TERM, 1990

SANDOZ PHARMACEUTICALS CORPORATION, ETC.,
PETITIONER

v.

UNITED STATES OF AMERICA

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT

BRIEF FOR THE UNITED STATES IN OPPOSITION

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QUESTION PRESENTED

Whether principles of collateral estoppel bar petitioner from relitigating issues that were decided in a prior action between the same parties under the Federal Food, Drug, and Cosmetic Act.

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-8a) is reported at 894 F.2d 825. The opinion of the district court (Pet. App. 9a-19a) is unreported. A related opinion of the United States District Court for the District of New Jersey (Pet. App. 22a-54a) is reported at 687 F. Supp. 946. The opinion of the Court of Appeals for the Third Circuit affirming the decision of the New Jersey court is reported at 871 F.2d 409.

JURISDICTION

The judgment of the court of appeals was entered on January 25, 1990. The petition for a writ of certiorari was filed on April 24, 1990. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

In this *in rem* action under the Federal Food, Drug, and Cosmetic Act (FDC Act), 21 U.S.C. 301 *et seq.*, both the court of appeals and the district court held that petitioner was barred by principles of collateral estoppel from litigating the question whether the drug Fiorinal with Codeine No. 3 (FWC No. 3) is a "new drug" within the meaning of 21 U.S.C. 321(p).[1] The courts below based their ruling on a prior judicial decision, in a separate action between petitioner and the United States, that the drugs Fiorinal with Codeine Nos. 1 and 2 (FWC Nos. 1 and 2) are "new drugs."

1. Petitioner produces FWC Nos. 1, 2, and 3 as treatments for tension headaches. Each drug contains 325 milligrams of aspirin, 40 milligrams of caffeine, and 50 milligrams of butalbital. Pet. App. 14a. In addition, FWC No. 1 contains 7.5 milligrams of codeine, FWC No. 2 contains 15 milligrams of codeine, and FWC No. 3 contains 30 milligrams of

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[1] Section 321(p) of Title 21, set out at Pet. App. 55a, defines a "new drug" as "[a]ny drug * * * the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." New drugs may not be marketed unless the Food and Drug Administration approves a new drug application pursuant to 21 U.S.C. 355(a). Section 355(a) is set out at Pet. App. 56a.

codeine. *Ibid.* Petitioner began marketing FWC in 1963 on the basis of informal advice from the Food and Drug Administration (FDA) that FWC-type products were not new drugs requiring a new drug application (NDA). *Id.* at 2a. Petitioner's original FWC products contained an additional ingredient, 130 milligrams of phenacetin, and contained only 200 milligrams of aspirin. In 1983, petitioner removed the phenacetin pursuant to an FDA directive and increased the dose of aspirin to its current level. *Id.* at 28a.

In 1968, the FDA revoked its informal opinions and required manufacturers to file an NDA for any product that is a "new drug" under 21 U.S.C. 321 (p).[2] See 21 C.F.R. 310.100. Petitioner subsequently submitted an abbreviated NDA pursuant to 21 C.F.R. 314.56, which permits abbreviated NDAs for duplicates of approved drugs and drugs that are "very closely related" to approved drugs. See 21 C.F.R. 314.56(c). The FDA rejected petitioner's abbreviated NDA with a statement that a full NDA was required. Pet. App. 2a. Petitioner continued to market its FWC products without an approved NDA.

In November 1984, the FDA sent petitioner a regulatory letter stating that continued marketing of FWC drugs without FDA approval would violate the FDC Act. Pet. App. 2a. Petitioner responded by submitting an NDA and renewing its request for an abbreviated procedure. The FDA found the NDA not approvable, and again rejected the request for an

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[2] This revocation resulted from amendments to the FDC Act that required the FDA to consider the effectiveness, as well as the safety, of most drugs placed in commerce since 1938. See *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 613-616 (1973).

abbreviated procedure. Petitioner informed the FDA of its position that FWC products were not new drugs, and submitted several studies that petitioner claimed supported its position. The FDA rejected petioner's view. *Ibid.*

2. In June 1986, the government seized several boxes of FWC No. 3 and filed this *in rem* forfeiture action in the District Court for the Southern District of Ohio, alleging that FWC No. 3 is a new drug that may not be introduced into interstate commerce absent an approved NDA. Pet. App. 3a. The government later filed a second forfeiture action in the District Court for the District of New Jersey, alleging that FWC Nos. 1 and 2 are new drugs. The parties submitted identical evidence with respect to the "new drug" status of the FWC drugs in both actions. *Ibid.*

a. The New Jersey district court ruled first. It granted summary judgment for the government in March 1988, holding that FWC Nos. 1 and 2 are new drugs. Pet. App. 53a. The court noted that, under the FDC Act, no product may be marketed without an approved NDA unless it is generally recognized as safe and effective for its intended use. Moreover, general recognition of a product's safety and effectiveness must be documented by at least the quality and quantity of evidence that would warrant FDA approval of an NDA. Pet. App. 25a, 27a (citing *Weinberger* v. *Rentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973)). An NDA, the court observed, must be supported by "adequate and well-controlled investigations, including clinical investigations." Pet. App. 25a (quoting 21 U.S.C. 355(d)). Accordingly, the court said, expert opinion as to the product's reputation in the scientific community must be based on well-controlled clinical studies, rather than uncon-

trolled data or the experts' personal experiences. Pet. App. 26a-27a (citing *Weinberger* v. *Hynson, Wescott & Dunning, Inc.*, 412 U.S. at 619). In the case of a "combination drug" such as the FWC compounds (that is, a drug with more than one active ingredient), an FDA regulation, 21 C.F.R. 300.50 (Pet. App. 59a-60a), requires evidence that each active ingredient makes a contribution to the claimed effect. The court explained that "the combination policy of 21 C.F.R. § 300.50 can only be met by studies of the particular drug product at issue or a drug having the same active ingredients which is demonstrably its bioequivalent." Pet. App. 51a.

Applying these statutory and regulatory standards, the New Jersey court held that the studies submitted by petitioner did not demonstrate that each of the active ingredients of the FWC drugs contributes to its effectiveness. The court found that four of the six studies submitted by petitioner tested the old FWC formulations, discontinued in 1983, that contained phenacetin and a smaller quantity of aspirin. Pet. App. 4a-5a n.1, 45a. The two studies that tested the current formula, the court found, did not evaluate the contribution of individual ingredients. *Id.* at 52a-53a. Furthermore, the court said, there was no study of any FWC formulation, old or new, that examined the contribution of the 40-milligram dose of caffeine to the claimed effectiveness of the products. *Id.* at 6a, 51a. And as to butalbital, the court found, the single study of its effectiveness had been conducted on the old FWC No. 2 formulation and therefore was not pertinent. *Id.* at 52a. Accordingly, the court held that FWC Nos. 1 and 2 were new drugs. *Id.* at 53a. The district court also denied petitioner's discovery requests on the ground that the information petitioner sought could not fill the gaps

in the required clinical investigations and therefore could not affect the outcome of the case.[3] *Ibid.*

b. In May 1988, the district court in this case held, on the basis of the prior decision in the New Jersey district court action between the same parties, that petitioner was collaterally estopped from litigating the question whether FWC No. 3 is a new drug. Applying the standards for collateral estoppel set out in *NAACP, Detroit Branch* v. *Detroit Police Officers Ass'n*, 821 F.2d 328, 330 (6th Cir. 1987), the district court determined that the New Jersey court had confronted

> the identical issues [that are] before this court. The lack of any study to determine the contribution of forty milligrams caffeine applies equally to Fiorinal with Codeine No. 3, as does the lack of studies concerning the contribution of butalbital. While the judgment of the New Jersey court did not specifically encompass Fiorinal with Codeine No. 3, the legal issues resolved by the court, particularly in regard to the non-codeine components of Fiorinal, which are identical regardless of the amount of codeine in the preparation, are the exact issues before this Court. The New Jersey court's findings as to these non-codeine components were not dependent upon or determined by the amount of codeine present and thus apply equally to Fiorinal with Codeine No. 3.

Pet. App. 15a-16a. The Ohio court further held that determination of the effectiveness of the non-codeine

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[3] Petitioner appealed to the Third Circuit, which unanimously affirmed the judgment of the district court. 871 F.2d 409 (1989). Petitioner did not seek review of the Third Circuit's judgment in this Court, and that judgment is now final. Petitioner has withdrawn FWC Nos. 1 and 2 from the market.

ingredients was necessary to the outcome of the New Jersey proceeding; that the New Jersey proceeding resulted in a final judgment on the merits; and that petitioner had a full and fair opportunity to litigate the issue in the New Jersey proceeding. *Id.* at 13a-17a. The Ohio court therefore granted summary judgment for the United States, entered a permanent injunction, and ordered that the seized FWC No. 3 be destroyed. *Id.* at 3a, 17a-18a.

4. The Sixth Circuit affirmed. Pet. App. 1a-8a. The court of appeals agreed that the four criteria of *Detroit Police Officers Ass'n, supra,* governed application of the collateral estoppel doctrine. Pet. App. 4a. As to the first criterion—identity of the issues in the two proceedings—the court held that the precise issue decided in the New Jersey litigation was presented by the Ohio litigation. "Both legal actions required identical showings that each ingredient [including the non-codeine ingredients] contributes to the claimed effect. In fact, in both the New Jersey and Ohio forums, [petitioner] defended the efficacy of its products with the same six studies and expert declarations." *Ibid.* As to the second criterion, the court concluded that the New Jersey court's finding (that the contribution of the non-codeine ingredients had not been shown) was necessary to the outcome of the New Jersey proceeding. *Id.* at 6a. Petitioner did not dispute that the New Jersey proceeding had resulted in a final judgment on the merits and therefore satisfied the third *Detroit Police Officers* criterion. *Id.* at 4a. And as to the fourth criterion, the court of appeals held that petitioner had been afforded a full and fair opportunity to litigate the relevant issue. Pet. App. 6a. Since the court of appeals concluded that the discovery sought by petitioner could not have led to a different result, it rejected

petitioner's contention that denial of discovery was unfair.[4] Pet. App. 7a-8a.

ARGUMENT

The decision of the court of appeals is correct and does not conflict with any decision of this Court or any other court of appeals. Accordingly, further review is unwarranted.

1. The question whether each of the non-codeine ingredients of the FWC drugs contributes to the claimed effect was litigated in the New Jersey action between petitioner and the United States. The determination of that issue was necessary to the outcome of the New Jersey case, because each component of a combination drug such as FWC must be shown to "make[] a contribution to the claimed effect[]." 21 C.F.R. 300.50(a). Because petitioner had a full and fair opportunity to litigate the issue in the New Jersey court, principles of collateral estoppel (issue preclusion) bar relitigation of the same issue in subsequent litigation between the same parties. See *Allen* v. *McCurry*, 449 U.S. 90, 95, 101 (1980).

a. Petitioner contends (Pet. 9-13) that principles of collateral estoppel should not apply to new drug determinations involving "different but related product[s]." Pet. 9. Because "[m]any * * * products contain similar ingredients but are distinctly different drugs," petitioner argues, collateral estoppel should not bar separate proceedings with respect to each such product. Pet. 9-10. Petitioner's argument fails in the context of this case. It is true that drugs

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[4] The court of appeals subsequently stayed its mandate pending this Court's action on the petition for a writ of certiorari. Pet. 9. In addition, an NDA for FWC No. 3 currently is pending before the FDA.

containing similar ingredients may have different effects. But it does not follow that where, as here, identical issues have been fully and fairly litigated in a prior proceeding between the same parties, collateral estoppel should not apply. Petitioner submitted identical studies to both courts, Pet. App. 3a, and those studies were found to be insufficient to establish any contribution to effectiveness by the non-codeine ingredients caffeine and butalbital. In these circumstances, collateral estoppel principles, which are rooted in the public interest in conserving judicial resources and avoiding duplicative litigation, are fully applicable.[5]

b. Petitioner incorrectly asserts (Pet. 10-13) that the decision in this case conflicts with this Court's decision in *United States* v. *Generix Drug Corp.*, 460 U.S. 453 (1983). *Generix* held that a generic drug with the same active ingredients as a previously approved prescription drug, but different inactive ingredients, is a new drug requiring an NDA. 460 U.S. at 459. Contrary to petitioner's contention, the application of collateral estoppel principles in this case was not based on an explicit or implicit holding that FWC 3 is the same drug as FWC 1 or FWC 2. Instead, the courts below focused specifically on FWC No. 3, and held that the determination in the New Jersey proceeding—that the evidence submitted by petitioner did not satisfy the requirement of 21

[5] There is no basis for petitioner's suggestion that the issue presented in this case will recur with any frequency. As petitioner correctly notes, "[t]his case represents the first time that collateral estoppel has been used to determine that a drug is a 'new drug,' " Pet. 9, and we are aware of relatively few instances in which a similar issue was presented by successive seizures of two products of the same manufacturer or distributor.

C.F.R. 300.50 that each ingredient be shown to contribute to a drug's claimed effect—was controlling with respect to the same evidence in the Ohio proceeding. Because petitioner failed to establish the contribution of either caffeine or butalbital, the larger dose of codeine in FWC No. 3 could not have led to a finding that FWC No. 3, but not FWC Nos. 1 and 2, is generally recognized as effective.

2. Petitioner also contends (Pet. 13-14)—citing *Yates* v. *United States*, 354 U.S. 298 (1957), overruled in part on other grounds, *Burks* v. *United States*, 437 U.S. 1 (1978)—that collateral estoppel should not apply in this case because the issues decided by the New Jersey court were not identical to the "ultimate" issues presented by the Ohio litigation.[6] *Yates* held only that evidentiary rulings in a political conspiracy trial would not be conclusive in a subsequent proceeding because the facts underlying those rulings "were so remote from the issues as to justify their exclusion from evidence." 354 U.S. at 338. Here, in contrast, the facts underlying the New Jersey proceeding were not at all remote from those of this case. Moreover, the effectiveness of the noncodeine ingredients was an "ultimate" rather than an "evidentiary" or "mediate" fact, because a new drug determination requires a demonstration of the contributions of each active ingredient. See *The Evergreens* v. *Nunan*, 141 F.2d 927, 928 (2d Cir.) (an "ultimate" fact is "one of those facts, upon whose combined occurrence the law raises the duty,

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[6] Petitioner raised this contention for the first time in its reply brief in the court of appeals. That court did not address the issue.

or the right, in question"), cert. denied, 323 U.S. 720 (1944).[7]

3. Petitioner next contends (Pet. 15-17) that application of collateral estoppel is inappropriate in this case because the New Jersey court decided an "unmixed question of law." According to petitioner, the result in the New Jersey action depended on that court's decision to apply the "identical drug" rule—*i.e.*, the rule that supporting studies must have been conducted on the identical drug in issue or its bioequivalent.[8] Pet. 15. Petitioner, citing *United States* v. *Moser*, 266 U.S. 236 (1924), argues that this was an unmixed question of law not subject to collateral estoppel principles. Petitioner's argument fails for several reasons.

As an initial matter, the New Jersey court's decision does not rest wholly on a rule that the requirements of 21 C.F.R. 300.50 can be met only by studies of the drug at issue or of its bioequivalent. Rather, the New Jersey court's decision with respect to the effectiveness of caffeine rests on petitioner's failure to offer any evidence regarding the contribution of 40 milligrams of caffeine to *any* FWC formulation, new or old, bioequivalent or not. Pet. App. 52a. This complete failure of proof with respect to caffeine required the court to conclude that FWC Nos. 1 and 2

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[7] See also Restatement (Second) of Judgments § 27 comment j (1982) ("The appropriate question * * * is whether the issue was actually recognized by the parties as important and by the trier as necessary to the first judgment. If so, the determination is conclusive between the parties in a subsequent action.").

[8] Under 21 U.S.C. 355(j)(7)(B), two drugs are "bioequivalent" if the rate and extent of absorption of the two drugs are not significantly different.

were new drugs whether or not it applied the independent drug rule.

In any event, petitioner's reliance on *United States* v. *Moser*, *supra*, is misplaced. As the court of appeals noted (Pet. App. 5a), this Court "severely limited" the exception to collateral estoppel principles for "unmixed questions of law" in *United States* v. *Stauffer Chemical Co.*, 464 U.S. 165, 170-172 (1984). The Court recognized in *Stauffer* that the exception for unmixed questions of law was "difficult to delineate," and stated that the exception applies only to "successive actions involving unrelated subject matter." 464 U.S. at 170, 171 (quoting *Montana* v. *United States*, 440 U.S. 147, 162, 163 (1979)). In both *Stauffer* and *Montana* v. *United States*, the Court had "no trouble" finding the exception inapplicable because of the "close alignment in both time and subject matter" of the two actions in those cases. See *Stauffer*, 464 U.S. at 170, 172; *Montana*, 440 U.S. at 163. Here, the two cases were pending simultaneously and the subject matter, involving products with the same active ingredients and the same quantities of noncodeine ingredients, was so closely aligned that petitioner submitted identical evidence in both proceedings. Thus, the exception for "unmixed" questions of law, whatever its scope, plainly does not apply in this case.

Moreover, the New Jersey court did not decide an "unmixed" question of law. As the court of appeals observed (Pet. App. 5a-6a), the New Jersey court's judgment was based on factual findings as to the validity and relevance of clinical studies, including the absence of critical bioequivalence data and data measuring the effect of 40 milligrams of caffeine. Pet. App. 50a-52a.

4. Petitioner's final contention (Pet. 18-19) is that, under principles articulated by this Court in *Parklane Hosiery Co.* v. *Shore*, 439 U.S. 322 (1979), it is unfair to apply collateral estoppel in this case. In support of this contention, petitioner suggests that experts might have concluded that FWC No. 3 is effective because it contains more codeine than FWC Nos. 1 or 2. Pet. 18. Petitioner simply overlooks the requirement that expert opinion must be based on well-controlled, clinical, published studies rather than on uncontrolled data or the experts' personal experience. See *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. at 619. Moreover, since petitioner failed to present any clinical studies of the effectiveness of caffeine in any FWC product, or of the effectiveness of butalbital in a current FWC formulation, no expert testimony concerning the effectiveness of FWC No. 3, however favorable to petitioner, could have established the effectiveness of those ingredients.

Petitioner's contention (Pet. 19) that it should have been permitted to engage in discovery fails for the same reason. Petitioner speculates that government experts might have admitted that they regard FWC No. 3 as effective because of its larger dose of codeine. But in the absence of clinical studies showing the product's effectiveness—including the contribution of each of its active ingredients—expert testimony could not alter the outcome of the case. See *United States* v. *225 Cartons, More or Less, of an Article or Drug*, 871 F.2d 409, 420 (3d Cir. 1989) (quoting *Upjohn Co.* v. *Finch*, 422 F.2d 944, 955 (6th Cir. 1970)) ("No amount of examination and

cross-examination can change the scientific studies and the data reported into something they are not.").[9]

CONCLUSION

The petitioner for a writ of certiorari should be denied.

Respectfully submitted.

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AUGUST 1990

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[9] In its petition for certiorari, petitioner abandons its argument that it lacked an adequate incentive to litigate the New Jersey action. The court of appeals properly rejected that argument, observing that sales of FWC Nos. 1 and 2 generated over $3 million a year for petitioner. See Pet. App. 7a. In addition, petitioner does not renew its argument that FWC No. 3 falls within an asserted exception to the requirement of well-controlled clinical investigation that petitioner argued was recognized in *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973). As the court of appeals noted in rejecting this argument (Pet. App. 8a), there is no exception to the requirement of clinical investigations, in *Bentex* or elsewhere, for long-used drugs such as the FWC products. See, *e.g.*, *Upjohn Co.* v. *Finch*, 422 F.2d 944 (6th Cir. 1970); *United States* v. *Articles of Food and Drug Coli-Trol 80 Medicated*, 372 F. Supp. 915 (N.D. Ga. 1974).

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